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| <u>L48</u> | rosaceae or vitaceae or umbelliferae | 1894 | <u>L48</u> |
| <u>L47</u> . | 145 not 13 | 30 | <u>L47</u> |

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END OF SEARCH HISTORY

Glycosylation

From Wikipedia, the free encyclopedia (Redirected from Glycosylated)

Glycosylation is the process or result of addition of saccharides to proteins and lipids. The process is one of four principal co-translational and post-translational modification steps in the synthesis of membrane and secreted proteins and the majority of proteins synthesized in the rough ER undergo glycosylation. It is an enzyme-directed site-specific process, as opposed to the non-enzymatic chemical reaction of glycation. Two types of glycosylation exist: N-linked glycosylation to the amide nitrogen of asparagine side chains and O-linked glycosylation to the hydroxy oxygen of serine and threonine side chains.

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Purpose

The polysaccharide chains attached to the target proteins serve various functions. For instance, some proteins do not fold correctly unless they are glycosylated first. Also, polysaccharides linked at the amide nitrogen of asparagine in the protein confer stability on some secreted glycoproteins. Experiments have shown that glycosylation in this case is not a strict requirement for proper folding, but the unglycosylated protein degrades quickly. Glycosylation may play a role in cell-cell adhesion (a mechanism employed by cells of the immune system), as well.

Mechanisms

There are various mechanisms for glycosylation, although all share several common features:

- Glycosylation is an enzymatic process
- The donor molecule is an activated nucleotide sugar
- The process is site-specific.

N-linked glycosylation

N-linked glycosylation is important for the folding of some of eukaryotic proteins. The N-linked glycosylation process occurs in eukaryotes and widely in archaea, but very rarely in bacteria.

For N-linked oligosaccharides, a 14-sugar precursor is first added to the asparagine in the polypeptide chain of the target protein. The structure of this precursor is common to most eukaryotes, and contains 3 glucose, 9 mannose, and 2 N-acetylglucosamine molecules. A complex set of reactions attaches this branched chain to a carrier molecule called dolichol, and then it is transferred to the appropriate point on the polypeptide chain as it is translocated into the ER lumen.

There are two major types of N-linked saccharides: high-mannose oligosaccharides, and complex oligosaccharides (Alberts et. al., Ch 13, pg 604). High-mannose is, in essence, just two N-acetylglucosamines with many mannose residues, often almost as many as are seen in the precursor oligosaccharides before it is attached to the protein. Complex oligosaccharides are so named because they can contain almost any number of the other types of saccharides, including more than the original two N-acetylglucosamines. Proteins can be glycosylated by both types of oligos on different portions of the protein. Whether an oligosaccharide is high-mannose or complex is thought to depend on its accessibility to saccharide-modifying proteins in the Golgi. If the saccharide is relatively inaccessible, it will most likely stay in its original high-mannose form. If it is accessible, then it is likely that many of the mannose residues will be cleaved off and the saccharide will be further modified by the addition of other types of group as discussed above.

The oligosaccharide chain is attached by oligosaccharyl transferase to asparagine occurring in the tripeptide sequence Asn-X-Ser or Asn-X-Thr, where X could be any amino acid except Pro. This sequence is known as a glycosylation *sequon*. After attachment, once the protein is correctly folded, the three glucose residues are removed from the chain and the protein is available for export from the ER. The glycoprotein thus formed is then transported to the Golgi where removal of further mannose residues may take place. However, glycosylation itself does not seem to be as necessary for correct transport targeting of the protein, as one might think. Studies involving drugs that block certain steps in glycosylation, or mutant cells deficient in a glycosylation enzyme, still produce otherwise-structurally-normal proteins that are correctly targeted, and this interference does not seem to interfere severely with the viability of the cells. Mature glycoproteins may contain a variety of oligomannose *N*-linked oligosaccharides containing between 5 and 9 mannose residues. Further removal of mannose residues leads to a 'core' structure containing 3 mannose, and 2 *N*-acetylglucosamine residues, which may then be elongated with a variety of different monosaccharides including galactose, *N*-acetylglucosamine, *N*-acetylglacosamine, fucose and sialic acid.

O-linked glycosylation

O-N-acetylgalactosamine (O-GalNAc)

O-linked glycosylation occurs at a later stage during protein processing, probably in the Golgi apparatus. This is the addition of N-acetyl-galactosamine to serine or threonine residues by the enzyme UDP-N-acetyl-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase, followed by other carbohydrates (such as galactose and sialic acid). This process is important for certain types of proteins such as proteoglycans, which involves the addition of glycosaminoglycan chains to an initially unglycosylated "proteoglycan core protein." These additions are usually serine O-linked glycoproteins, which seem to have one of two main functions. One function involves secretion to form components of

the extracellular matrix, adhering one cell to another by interactions between the large sugar complexes of proteoglycans. The other main function is to act as a component of mucosal secretions, and it is the high concentration of carbohydrates that tends to give mucus its "slimy" feel. Proteins that circulate in the blood are not normally *O*-glycosylated, with the exception of IgA1 and IgD (two types of antibody) and C1-inhibitor.

O-fucose

O-fucose is added between the second and third conserved cysteines of EGF-like repeats in the Notch protein, and possibly other substrates by GDP-fucose protein O-fucosyltransferase 1, and to Thrombospondin repeats by GDP-fucose protein O-fucosyltransferase 2. In the case of EGF-like repeats, the O-fucose may be further elongated to a tetrasaccharide by sequential addition of N-acetylglucosamine (GlcNAc), galactose, and sialic acid, and for Thrombospondin repeats, may be elongated to a disaccharide by the addition of glucose. Both of these fucosyltransferases have been localized to the endoplasmic reticulum, which is unusual for glycosyltransferases, most of which function in the Golgi apparatus.

O-glucose

O-glucose is added between the first and second conserved cysteines of EGF-like repeats in the Notch protein, and possibly other substrates by an unidentified O-glucosyltransferase.

O-N-acetylglucosamine (*O*-GlcNAc)

O-GlcNAc is added to serines or threonines by O-GlcNAc transferase. O-GlcNAc appears to occur on serines and threonines that would otherwise be phosphorylated by serine/threonine kinases. Thus, if phosphorylation occurs, O-GlcNAc does not, and vice versa. This is an incredibly important finding because phosphorylation/dephosphorylation has become a scientific paradigm for the regulation of signaling within cells. A massive amount of cancer research is focused on phosphorylation. Ignoring the involvement of this form of glycosylation which clearly appears to act in concert with phosphorylation means that a lot of current research is missing at least half of the picture. O-GlcNAc addition and removal also appear to be key regulators of the pathways which are deregulated in diabetes mellitus. The gene encoding the O-GlcNAc removal enzyme has been linked to non-insulin dependent diabetes mellitus. It is the terminal step in a nutrient sensing hexosamine signaling pathway.

GPI anchor

A special form of glycosylation is the *GPI anchor*. Although this is a form of glycosylation, the result is a hydrophobic side chain, making GPI anchoring quite similar to prenylation.

C-mannosylation

A mannose sugar is added to tryptophan residues in Thrombospondin repeats. This is an unusual modification both because the sugar is linked to a carbon rather than a reactive atom like a nitrogen or oxygen and because the sugar is linked to a tryptophan residue rather than an asparagine or serine/threonine.

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| <u>L4</u> | plant near2 extracts | 25521 | <u>L4</u> |
|-------------|------------------------------------------------------|---------|-------------|
| <u>L3</u> | ll not L2 | 109 | <u>L3</u> |
| <u>L2</u> | @pd>20021023 | 8437209 | <u>L2</u> . |
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END OF SEARCH HISTORY